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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MITCHELL, GREGORY W	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 08/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/890,969	LUU ET AL.	
	Examiner	Art Unit	
	Gregory W. Mitchell	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the Remarks and Amendments filed June 24, 2005. Claims 10-12, 16-18, and 22-23 have been amended. Claims 10-29 are pending and are examined herein. Applicant's Amendments have necessitated the withdrawal of the rejections and objections set forth in the previous Office Action. The following rejections now apply.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of ALS with trimethyl substituted cyclohexenone compounds, does not reasonably provide enablement for the treatment of ALS with non, mono, or bis methyl substituted cyclohexenones. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547,

the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1). ***The Nature of the Invention***:

The rejected claim(s) is/are drawn to an invention which pertains to a method of treating ALS with various cyclohexenones.

(2). ***Breadth of the Claims***:

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The claims encompass a treatment comprising the administration of cyclohexenones comprising anywhere from 0-3 methyl substituents.

(3). ***Guidance of the Specification***:

The guidance given by the specification as to what types of cyclohexenones would be useful in a method of the instant invention is limited. Of the chains comprising an X group of formula 1 of greater than 14 carbons, only the trimethyl substituted cyclohexenones are disclosed in the specification.

(4). ***Working Examples***:

For compounds with an X group greater than 14 carbons, the working examples show successful neurite-extension effects by utilizing the tri-methyl substituted cyclohexenones.

(5). ***State of the Art***:

The state of the art with regard to the treatment of ALS is underdeveloped. Girianda-Junges et al. (*Tetrahedron*, 54, 7735-7748) teaches the neurite outgrowth capabilities of various cyclohexenones. Disclosed therein are non, mono, and bis methyl substituted cyclohexenones (p. 7736). Of these, Girianda-Junges et al. teaches that those compounds wherein the chain corresponding to the X group of formula 1 of the compounds claimed herein is greater than 14 carbons in length, the activity disappears and that the activity is replaced with neurotoxicity (p. 7740, Table 1).

(6). ***Predictability of the Art***:

It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839 (1970).

Moreover, one of skill in the art would recognize that it is highly unpredictable in regard to therapeutical effects, side effects, and especially serious toxicity that may be generated by drug-drug inerteractions when and/or after adminstering to a host (e.g., a human) any compounds represented by formula 1, particularly in view of the teachings of Girianda-Junges et al. that non, mono, and bis methyl substituted cyclohexenones

with an X group of greater than 14 carbons leads to neurotoxicity. See "Goodman & Gilman's The Pharmacological Basis of Therapeutics" regarding possible drug-drug interactions (9th ed., 1996), page 51 in particular. *Goodman & Gilman* teaches that "The frequency of significant beneficial or adverse drug interactions is unknown" (see the bottom of the left column of page 51) and that "Recognition of beneficial effects and recognition of and prevention of adverse drug interactions require a thorough knowledge of the intended and possible effects of drugs that are prescribed" and that "The most important adverse drug-drug interactions occur with drugs that have serious toxicity and a low therapeutic index, such that relatively small changes in drug level can have significant adverse consequences" (see the right of page 51) (emphasis added).

(7). ***The Quantity of Experimentation Necessary***:

The specification fails to provide sufficient support of the broad use of any compound represented by formula 1. As a result, one of skill in the art would be forced to perform an exhaustive search for the embodiments of any drugs having the function recited in the instant claim suitable to practice the claimed invention.

Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 10-29 rejected under 35 U.S.C. 103(a) as being unpatentable over Girianda-Junges et al. (*Tetrahedron*, 54, 7735-7748) and Luu et al. (USPN 6228893) in view of each of Borg (USPN 5447959), Pruss (USPN 5731354), and Rosen et al. (*Nature*, 362, 59-62).

Girianda-Junges et al. teaches cyclohexenones as small lipids which are able to mimic the biological activity of naturally occurring protein neurotrophic factors which are, in turn, taught as potential therapeutic agents for the treatment of neurodegenerative disorders (p 7735). The cyclohexenones wherein the straight chain aliphatic substituent is between 10 and 14 carbon atoms were taught to be neurotrophic by inducing neurite outgrowth, which is taught to be associated with neuronal differentiation and neuron survival (pp 7736 and 7740). Girianda-Junges et al. does not specifically teach the compounds, as claimed or the treatment of the specific neurodegenerative disorder, ALS.

Luu et al. teaches cyclohexenones of formula 1 with an X group of between 10 and 18 carbon atoms as useful in the treatment of disorders such as Alzheimer's disease and dementia (neurodegenerative disorders) (Abstract; col. 2, lines 1-42). Luu et al. does not specifically teach the treatment of ALS.

Borg teaches the treatment of neuro-degenerative illnesses with derivatives of long-chain fatty alcohols (Abstract, col. 13, lines 17-21). Exemplified are trimethylcyclohexenonyl compounds substituted with both saturated and unsaturated branched fatty alcohols (col. 19, line 55-col. 21, line 53). Borg teaches that diseases such as Alzheimer's disease, Parkinson's disease, Huntington's chorea and amyotrophic lateral sclerosis are disorders associated with the progressive disappearance of certain neurons (col. 1, lines 49-53). Borg teaches that the compounds taught therein promote neuronal differentiation as well as survival of neurons (col. 25, lines 55-58). The agents of Borg are administered as pharmaceutical compositions by various means, preferably orally (col. 15, lines 4-11). Neuro-degenerative disorders are taught to be treatable in dosages of 0.1 mg/kg/day to 10 mg/kg/day (col. 28, lines 8-19). These dosages correlate to 7.0 mg/day to 700 mg/day for an average individual weighing 70 kg.

Pruss teaches a fatty alcohol derivative for the treatment of neurodegenerative disorders, including stroke, Alzheimer's disease, multiple sclerosis and amyotrophic lateral sclerosis (col. 4, lines 26-30). The fatty acid alcohol derivatives of Pruss are taught to act as lipids and to treat the neurodegenerative disorders above by inhibiting the degeneration of neural cells leading to premature apoptosis and cell death (col. 4, lines 18-25 and lines 40-49).

Rosen et al. teaches that mutations in superoxide dismutase gene are associated with familial amyotrophic lateral sclerosis.

It would have been obvious to one of ordinary skill in the art at the time of the invention to treat specifically treat amyotrophic lateral sclerosis with the specific compounds as instantly claimed because (1) Girianda-Junges et al. teaches the use of homologues of the instantly claimed compounds in the treatment of neurodegenerative disorders (it is noted, for example, that a 2-methyl tetradecyl branched alkyl would meet the instant claims) and absent unexpected properties, homologs are generally considered to be obvious (*In re Hass*, 141 F.2d 127, 60 USPQ 548 (CCPA 1944); *In re Henze*, 85 USPQ 261 (CCPA 1950)); (2) Luu et al. teaches the compounds as instantly claimed as useful for the treatment of disorders such as Alzheimer's and dementia (neurodegenerative disorders); (3) Borg teaches a genus of compounds that encompasses the instant compounds for the treatment of neurodegenerative disorders, in general; and (4) Pruss teaches that amyotrophic lateral sclerosis and Alzheimer's disease are both neuro-degenerative disorders that are known in the art to be treatable by similar means. It is also noted that (1) Borg and Pruss both teach that amyotrophic lateral sclerosis is associated with neuron death; (2) Borg teaches the treatment of neurodegenerative disorders with compounds that encompass the instantly claimed compounds; (3) Pruss teaches that the fatty alcohol derivatives disclosed therein are useful for inhibiting premature apoptosis; and (4) Girianda-Junges et al. teaches that the cyclohexenones as instantly claimed are known to be neurotrophic and that such actions are associated with neuron survival. One would have been motivated to specifically treat amyotrophic lateral sclerosis with the compounds as instantly claimed

because of an expectation of success in treating various specific neuro-degenerative disorders with fatty alcohol derivatives, as taught by both Borg and Pruss.

It is noted that, as taught by Rosen et al., amyotrophic lateral sclerosis is a disorder associated with a mutation in a superoxide dismutase gene. Accordingly, the treatment of amyotrophic lateral sclerosis is obviously a treatment for a disorder associated with a mutation in a superoxide dismutase gene.

Response to Arguments

Applicant's arguments dated June 24, 2005, in conjuncture with the amendments filed therewith, are sufficient to overcome the rejections and objections of the Office Action dated February 24, 2005. Applicant's arguments with respect to the instant rejections are not persuasive.

Applicant argues that Borg et al. "neither teaches nor suggests the use of the compound of the present claims for the treatment of amyotrophic lateral sclerosis." This argument is not persuasive because the instantly claimed compounds are a subgenus within the genus taught by Borg et al. to be useful for the same purposes as herein envisioned, particularly the di and tri methyl substituted cyclohexenones. See col. 3, lines 52-65).

Applicant argues that Girlanda-Yunges et al. is no longer applicable because "the claims are now limited to X being C15-28 linear or branched alkylene group or a C15 linear or branched alkenylene group." This argument is not persuasive because, as discussed above, the claims encompass branched alkylene groups. Therefore, the

linear portion of the alkylene could be C14, with a methyl substitution at some point along the chain. Accordingly, one of ordinary skill in the art would have expected a methyl branched homolog to have the same effect as the C14 linear chain. Accordingly, it is Examiner's position that Girlanda-Yunges et al. teaches away from the C15 linear homolog, but not away from a C15 branched homolog.

Applicant's argument that "Pruss ... uses a compound which is completely different from the compounds of the present claims" is not persuasive because Pruss has been used, primarly, to show that neurodegenerative disorders, such as Alzheimer's Disease, ALS, etc., are known in the art to be similarly treated.

Applicant's arguments as they pertain to Rosen et al. are not persuasive because Examiner has relied on Rosen et al. only to show that ALS is known in the art to be associated with a mutation in a superoxide dismutase gene.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory W Mitchell whose telephone number is 571-272-2907. The examiner can normally be reached on M-F, 8:30 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

gwm

SREENI PADMANABHAN
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